

Application No. 10/581,106
Reply Dated October 28, 2011
Reply to Restriction Requirement of August 31, 2011

Amendment to the Specification:

On page 15 of the specification, beginning at line 28 through page 16, ending at line 12, please replace the following two paragraphs:

In another embodiment, the CAB is an MDTA as described in PCT Application Number US03/18200, filed ~~June 12, 2002~~ June 9, 2003 and incorporated herein by reference in its entirety. Some of the CAB molecules of the present invention have been shown to preferentially bind to a microtarget present on a target relative to binding of a non-target. The difference in binding can be caused by any difference between the target and non-target such as, for example, a difference in pH, oxygen pressure, concentration of solutes or analytes (e.g., lactic acid, sugars or other organic or inorganic molecules), temperature, light or ionic strength. Preferential binding of the CABs of the current invention can be used to bind to a microtarget under a desired set of conditions, identify a target *in vitro*, *ex vivo*, *in situ* or *in vivo* (e.g., a target tissue in a subject), kill a target cell or tissue, convert a prodrug into an active drug in or near a target tissue. It also can be used as surface catalysts, for example, a targeted laccase. Other uses include, e.g., targeted generation of a compound (e.g., H₂O₂ from glucose) and the targeted destruction of compounds (e.g., a metabolite or signalling molecule from a particular tissue).

In one embodiment, the CAB is selected, made or modified using an affinity maturation method, e.g., as described in ~~PCT application, filed June 12, 2002~~ U.S. Provisional Application No. 60/388,387, filed June 12, 2002 and incorporated herein by reference in its entirety.

On page 22 of the specification, beginning at line 16 through page 23, ending at line 21, please replace the following two paragraphs:

For example, *E. coli* is typically transformed using derivatives of pBR322, described by Bolivar *et al.*, 1977, Gene 2:95. Plasmid pBR322 contains genes for ampicillin and tetracycline resistance. These drug resistance markers can be either retained or destroyed in constructing the desired vector and so help to detect the presence of a desired recombinant. Commonly used

procaryotic control sequences, i.e., a promoter for transcription initiation, optionally with an operator, along with a ribosome binding site sequence, include the β -lactamase (penicillinase) and lactose (lac) promoter systems, *see Chang et al.*, 1977, *Nature* 268:1056 275: 617-624 (1978) and Goedell et al., *Nature* 281: 544-548 (1979), the tryptophan (trp) promoter system, *see Goeddel et al.*, 1980, *Nuc. Acids Res.* 8:4057, and the lambda-derived P_L promoter, *see Shimatake et al.*, 1981, *Nature* 292:128, and gene N ribosome binding site (N_{RBS}). A portable control system cassette is set forth in U.S. Patent No. 4,711,845, issued December 8, 1987. This cassette comprises a P_L promoter operably linked to the N_{RBS} in turn positioned upstream of a third DNA sequence having at least one restriction site that permits cleavage within six base pairs 3' of the N_{RBS} sequence. Also useful is the phosphatase A (phoA) system described by Chang *et al.*, in European Patent Publication No. 196,864, published October 8, 1986. However, any available promoter system compatible with procaryotes can be used to construct a expression vector of the invention.

In addition to bacteria, eucaryotic microbes, such as yeast, can also be used as recombinant host cells. Laboratory strains of *Saccharomyces cerevisiae*, Baker's yeast, are most often used, although a number of other strains are commonly available. While vectors employing the two micron origin of replication are common, *see Broach*, 1983, *Meth. Enz.* 101:307, other plasmid vectors suitable for yeast expression are known. *See, e.g.*, *Stinchcomb et al.*, 1979, *Nature* 282:39; Tschumper et al., 1980, *Gene* 10:157; and *Clarke et al.*, 1983, *Meth. Enz.* 101:300. Control sequences for yeast vectors include promoters for the synthesis of glycolytic enzymes. *See Hess et al.*, 1968, *J. Adv. Enzyme Reg.* 7:149; *Holland et al.*, 1978, *Biotechnology* 17:4900; and *Holland et al.*, 1981, *J. Biol. Chem.* 256:1385. Additional promoters known in the art include the promoter for 3-phosphoglycerate kinase, *see Hitzeman et al.*, 1980, *J. Biol. Chem.* 255:2073, and those for other glycolytic enzymes, such as glyceraldehyde 3-phosphate dehydrogenase, hexokinase, pyruvate decarboxylase, phosphofructokinase, glucose-6-phosphate isomerase, 3-phosphoglycerate mutase, pyruvate kinase, triosephosphate isomerase, phosphoglucose isomerase and glucokinase. Other promoters

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that have the additional advantage of transcription controlled by growth conditions are the promoter regions for alcohol dehydrogenase 2, isocytochrome C, acid phosphatase, degradative enzymes associated with nitrogen metabolism and enzymes responsible for maltose and galactose utilization.

On page 70 of the specification, lines 16 though 21, please replace the following paragraph:

All patents and publications mentioned in the specification are indicative of the levels of those skilled in the art to which the invention pertains. All patents and publications are herein incorporated by reference to the same extent as if each individual publication was specifically and individually indicated to be incorporated by reference. Specifically, ~~Attorney Docket Number(s) 839 et seq (e.g., 839-2P)~~ U.S. Provisional Application No. 60/562,386, filed April 15, 2004, and U.S. Provisional Application No. 60/636,002, filed December 14, 2004 are herein incorporated by reference, herein, in their entirety, including any drawings.